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June 17, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 2003N-0076; Food Labeling: *Trans* Fatty Acids in Nutrition Labeling; Reopening of the Comment Period; 69 Fed. Reg. 9559 (Mar. 1, 2004)

The following comments are provided in response to the Food and Drug Administration (FDA) March 1, 2004 Advanced Notice of Proposed Rulemaking (ANPR) on *trans* fatty acids in nutrition labeling. These comments are submitted on behalf of the E.I. DuPont de Nemours and Company (DuPont), Agriculture and Nutrition Businesses. Founded in 1802, DuPont is a science company, delivering science-based solutions that make a difference in people's lives around the world in areas such as food and nutrition, health care, apparel, safety and security, home and construction, electronics, and transportation. DuPont is committed to the safety of all products at all stages of development and production. DuPont Agriculture & Nutrition leverages science and food value chain knowledge to increase the quality, quantity and safety of the global food supply. The DuPont Agriculture & Nutrition businesses include: Pioneer Hi-Bred International, the world's largest seed business; DuPont Crop Protection, a global provider of herbicides, fungicides and insecticide products and services; Qualicon, a microbial diagnostic business; Liqui-Box, a leading manufacturer of liquid packaging systems; Food Industry Solutions, a food process consulting business, and two food industry joint ventures: The Solae Company™, providing better ingredients for better living and 8th Continent™, a leader in soymilk.

Summary

To aid consumer education regarding the significance of *trans* fat and saturated fat in the total daily diet, and to facilitate reformulation of products with healthful alternatives to *trans* fat-containing ingredients, DuPont urges FDA to take the following steps as soon as possible:

- Reject establishment of a combined daily value for *trans* fat and saturated fat, which would improperly link stearate, a cholesterol-neutral fatty acid, with *trans* fat,

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- Permit stearate to be declared separately in the Nutrition Facts panel, apart from saturated fat, and
- Take into account the need to facilitate responsible reformulation in setting other regulatory policies concerning *trans* and other fatty acids (e.g., when establishing criteria for claims).

The basis for each of these requests is discussed more fully below.

Introduction—Advances in Fatty Acid Science

The ANPR raises fundamental questions regarding the relationship between *trans* fat and saturated fat, and how information about these fatty acids should be conveyed in food labeling. For many years, fatty acids have been categorized for consumer purposes on the basis of their chemical structure as saturated fatty acids or as unsaturated fatty acids (mono- or polyunsaturated). As part of this paradigm, saturated fats have been widely conveyed as uniformly detrimental.

With advances in nutrition science, however, a better understanding of the health effects of individual fatty acids has emerged. The effects of specific dietary fatty acids on the risk of coronary heart disease (CHD) are now sufficiently understood to support a labeling policy that permits distinctions to be drawn between saturated fatty acids with detrimental effects and those with neutral or beneficial effects. Literature and data concerning the beneficial effect of stearate, in particular, were described in the recent work of Mensink et al., who conducted a meta-analysis of 60 controlled trials and calculated the effects of the amount and type of fat on the ratio of total cholesterol to high density lipoprotein (HDL) cholesterol and other lipids. ^{1/}

Of particular interest, Mensink reported changes in low density lipoprotein (LDL) cholesterol when 1% of energy as carbohydrate is exchanged for specific fatty acids, including laurate, myristate, palmitate, stearate, oleate, and polyunsaturated fatty acids (PUFAs). These data, which are represented graphically in Attachment A, demonstrate that individual fatty acids may be categorized as raising or lowering LDL cholesterol. Significantly, the effects of stearate, a saturated fatty acid, were most appropriately classified with PUFAs and oleate, not with other saturated fatty acids. This meta-

^{1/} Mensink et al. (2003). Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am. J. Clin. Nutr.* 77:1146-55.

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analysis supports and confirms a considerable body of evidence indicating that stearate is cholesterol-lowering or neutral. Indeed, the status of stearate as cholesterol-lowering or neutral was discussed and recognized at the April 27-28 meeting of the Nutrition Subcommittee of the Food Advisory Committee.

Consumer messages concerning dietary lipids can and should advance to reflect this important understanding of stearate. Significantly, the foundation for consumer messages concerning individual fatty acids is in place: consumers have long been taught that LDL cholesterol is "bad" cholesterol, and HDL cholesterol is "good" cholesterol.^{2/} Moreover, nutrition labeling has permitted identification of fat generally as saturated, monounsaturated, and polyunsaturated, so the notion that there are different categories of fat is firmly established. Now that the LDL-HDL message is accepted and understood, and broad categories of fatty acids have been identified, consumers are in a position to understand the next generation of dietary lipids messaging—that individual dietary fatty acids, including some saturated fats, may be either cholesterol-raising or cholesterol-lowering.

This increased understanding of fatty acid science needs to be reflected in the continuing evolution of consumer messages about dietary cholesterol and CHD prevention. There is a natural and logical progression of these messages, as illustrated in Attachments B-D. Attachment B depicts the first distinction: between LDL ("bad") cholesterol and HDL ("good") cholesterol, a distinction now well understood and accepted, as noted above. Attachment C shows the next step: the distinction that some types of dietary fatty acids are cholesterol-raising (saturated fat and, more recently, *trans* fat) while others are cholesterol-lowering (unsaturated fats, poly and mono). The next step, which DuPont is now advocating, is shown in Attachment D—namely, to distinguish among the different saturated fatty acids for purposes of identifying those for which intake should be decreased (laurate, myristate, and palmitate) and those for which dietary intake should be increased (stearate).

Accordingly, this advance in fatty acid science—and the resultant need for consumer dietary messages to evolve consistent with the science—lead DuPont to make the following comments on FDA's ANPR, which DuPont believes warrant FDA's serious attention.

^{2/} See, e.g., Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (2001). *J. Am. Med. Assoc.* 285: 2486-2497.

Not All Saturated Fats Are Created Equal: Food Labeling Should Facilitate Identification of Stearate

FDA is seeking comment as to whether a joint daily value should be established for saturated fat and *trans* fat. In support of a combined daily value, similarities between some saturated fatty acids and *trans* fatty acids, namely, adverse effects on LDL cholesterol, have been emphasized.

DuPont believes strongly that a joint daily value should not be established. By law, nutrition labeling must be conveyed to the public "in a manner which enables the public to readily observe and comprehend such information and to understand its relative significance in the context of a total daily diet." ^{3/} If a single daily value is presented for *trans* fat and all saturated fatty acids, it sends the undeniable message that these substances play a similar role in the total daily diet. This result emphasizes the similarities over key differences, with negative implications for public health.

Significantly, a combined daily value would fail to account for the beneficial effects of stearate, which were recognized at the Nutrition Subcommittee meeting. In addition, a combined daily value would almost certainly be based on CHD risk, at a time when emerging data suggest other endpoints may be relevant for *trans* fat, including possible adverse effects on glucose control. By implying that *trans* fat and all types of saturated fat are similar, a combined daily value would, therefore, fail to convey the biological significance of *trans* fat and saturated fatty acids in the total daily diet. Indeed, it would actually have the potential to confuse consumers and frustrate nutrition education efforts that increasingly point to the individual nutritional pharmacology of fatty acids, such as stearate. Moreover, the combination of a daily value for *trans* fat and saturated fat would provide a strong disincentive for reformulation with stearate-containing products.

Responsible Reformulation Is Needed

DuPont urges FDA to exercise leadership and take policy and other actions that will encourage reformulation of products to reduce or eliminate *trans* fat in a healthful manner. As was discussed at the Nutrition Subcommittee meeting, if *trans* fats are simply replaced by saturated fats without regard to amount or the overall fatty acid profile of a product, the net effect on public health may well be detrimental. Care must

^{3/} Nutrition Labeling and Education Act of 1990 (NLEA) § 2(b)(1)(A).

be exercised to ensure that FDA's labeling policies, as well as efforts to reformulate, do not lead to unintended negative consequences.

Responsible reformulation requires time and careful attention to detail. Two considerations are of particular importance. First, the effects of fats that are proposed as replacements to *trans* fats must be thoroughly evaluated from both a clinical safety and nutritional perspective. The analysis should be a proactive one that factors in a broad spectrum of clinical endpoints in addition to effects on lipoprotein metabolism or CHD. In clinical studies on *trans* fatty acids, for example, adverse effects on glucose control and inflammatory proteins are surfacing, underscoring the need to consider outcome variables beyond serum lipids when evaluating the potential health impact of fatty acids.

Second, reformulation must be viewed in a holistic manner, taking into account the overall fatty acid profile of individual products as well as the total diet, and acknowledging the dynamic forces that may be in play. For instance, potential negative effects of individual fatty acids must be evaluated in light of positive influences of other fatty acids that may be present in a product or encouraged for consumption, such as the n-3 PUFA, docosahexaenoic acid (DHA). ^{4/}

^{4/} With specific regard to stearate, DuPont acknowledges the recent work of Baer et al. concerning the effect of individual fatty acids on plasma markers of inflammation (Baer et al., 2004, Dietary fatty acids affect plasma markers of inflammation in healthy men fed controlled diets: a randomized crossover study. *Am. J. Clin. Nutr.* 79: 969-73). This preliminary study suggests that dietary fatty acids can modulate markers of inflammation, which may predict cardiovascular disease, and that stearate may have an adverse effect on select markers. This study, however, must be viewed in light of the totality of available evidence concerning the role of fatty acids as well as the role of inflammation as a risk factor for CHD. Significantly, the changes attributed to stearate in this study, while in a negative direction, were small in magnitude, within the clinical norm, and well below the level associated with increased risk of cardiovascular disease (Pearson et al., 2003, Markers of Inflammation and Cardiovascular Disease: Application to Clinical and Public Health Practice. A Statement for Healthcare Professionals From the Centers for Disease Control and Prevention and the American Heart Association in *Circulation* 107: 499-511). In addition, the article fails to account for the positive and offsetting influence of n-3 fatty acids, for which anti-inflammatory effects have been reported. For instance, Madsen, et al. reported an inverse relationship between the content of DHA in plasma granulocytes and C-Reactive Protein (Madsen et al., 2001, C-Reactive Protein, Dietary n-3 Fatty Acids, and the Extent of Coronary Artery Disease. *Am. J. Cardiol.* 88:1139-1142). The need for a holistic approach to dietary fatty acids

DuPont believes that stearate-containing fats and oils hold great promise for responsible reformulation. Stearate is a saturated fatty acid and as such is oxidatively stable, has a high melting point, and can be used for baking and frying applications. Its use provides additional flexibility for food companies to offer healthy products while retaining the oil functionality and flavor characteristics needed for making and storing food products. As noted previously, there is now widespread recognition in the scientific community, based on the literature and a comprehensive meta-analysis, indicating that stearate has a neutral or lowering effect on LDL cholesterol. To provide an incentive for further exploration of the use of stearate-containing products, voluntary declaration of stearate—outside of the saturated fats line—should be permitted. Combining all saturated fats and *trans* fats into a single daily value would frustrate and undermine this objective.

Precedent for Stearate Labeling

The separate declaration of stearate in food labeling is not only firmly rooted in science; it is also supported by regulatory precedent. Since 1993, the U.S. Department of Agriculture (USDA) has permitted the voluntary declaration of stearic acid in nutrition labeling, on the basis of what was at that time described as a “near consensus that . . . stearic acid does not have the same serum cholesterol-raising effect as the three other saturated fatty acids—myristic, palmitic, and lauric.” 5/ What was a “near consensus,” in 1993, has now reached a level of meaningful scientific agreement.

Precedent for further specificity in the labeling of individual fatty acids is also found in the recently accepted notification for nutrient content claims for the n-3 fatty acids DHA, eicosapentaenoic acid (EPA), and alpha-linolenic acid (ALA), which provides for claims such as the following: “Excellent Source of DHA omega-3. Contains ____ mg of DHA per serving, which is ____% of the Daily Value for ____ DHA (130 mg).” 6/ This precedent

and reformulation is also underscored by the recent work of Jenkins et al., (2003) Effects of a Dietary Portfolio of Cholesterol-Lowering Foods vs. Lovastatin on Serum Lipids and C-Reactive Protein *J. Am. Med. Assoc.* 290: 502-510.

5/ 58 Fed. Reg. 632 (Jan. 6, 1993); 9 C.F.R. §§ 317.309(d), 381.409(d).

6/ Alaska General Seafoods et al., Notification for a Nutrient Content Claim Based on An Authoritative Statement; Nutrient Content Claims for DHA, EPA, and ALA (Specific Omega-3 Fatty Acids) (Jan. 16, 2004) (effective May 2004).

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helps to establish the increasing significance of individual fatty acids in public health, and demonstrates the foundation for consumer communications conveying their specific identity. Consumers, therefore, will become increasingly comfortable with the concept of specific fatty acids in human nutrition.

Summary and Recommendations

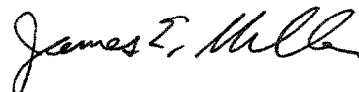
Because nutrition labeling serves as an important and credible source of nutrition information, it must facilitate consumer education that is based on science. In the case of fatty acids, public health would be served by labeling that permits identification of individual fatty acids—specifically, stearate—in the Nutrition Facts panel and elsewhere on the label. Of even greater importance, nutrition labeling must not cause further confusion by grouping nutrients together in a way that suggests they are similar from a dietary perspective, when the science indicates that they are not.

Accordingly, to aid consumer education and responsible reformulation, DuPont urges the agency to (1) not establish a combined daily value for *trans* fat and saturated fat, which improperly links stearate with *trans* fat, (2) permit stearic acid to be declared separately in the Nutrition Facts panel, apart from saturated fat, and (3) take into account the need to facilitate responsible reformulation in setting other regulatory policies concerning *trans* and other fatty acids (e.g., when establishing criteria for claims).

* * * * *

Dupont appreciates this opportunity to offer comments concerning fatty acid labeling. If it would be useful to discuss the points made in these comments, or if additional information is desired, please contact us.

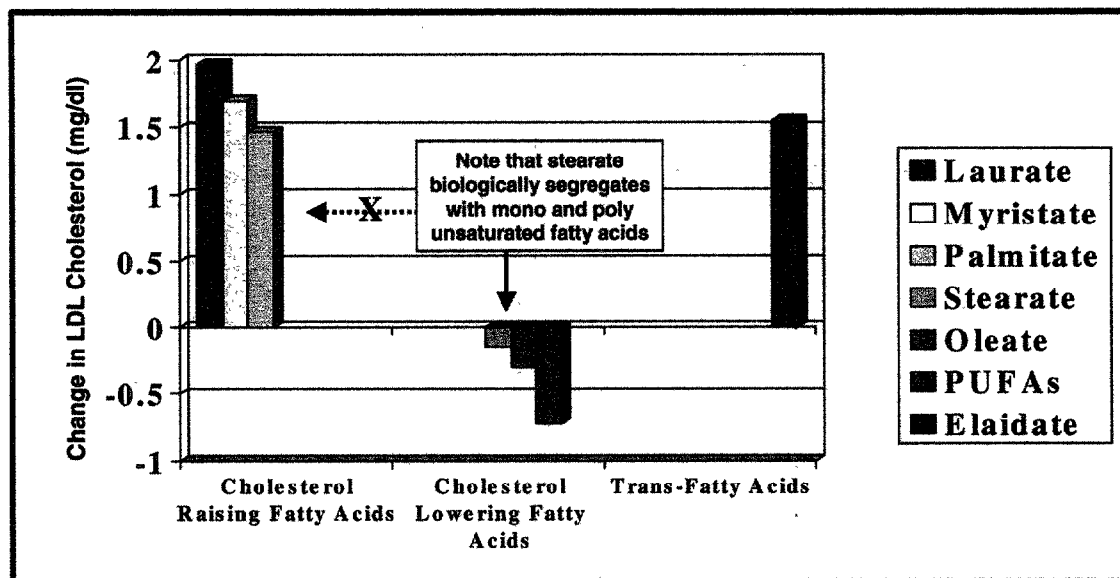
Sincerely,

A handwritten signature in cursive script, appearing to read "James E. Miller".

James E. Miller, Ph.D.
Vice President
DuPont Agriculture & Nutrition

Attachment A

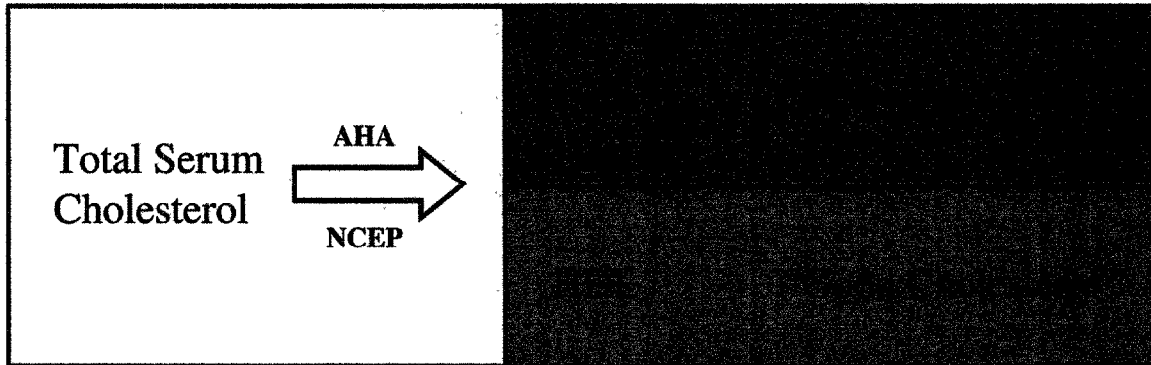
Change in LDL Cholesterol when Exchanging 1% of Energy as Carbohydrate for Specific Fatty Acids



Adapted from Mensink et al (2003) *Am J Clin Nutr* 77:1146

Attachment B

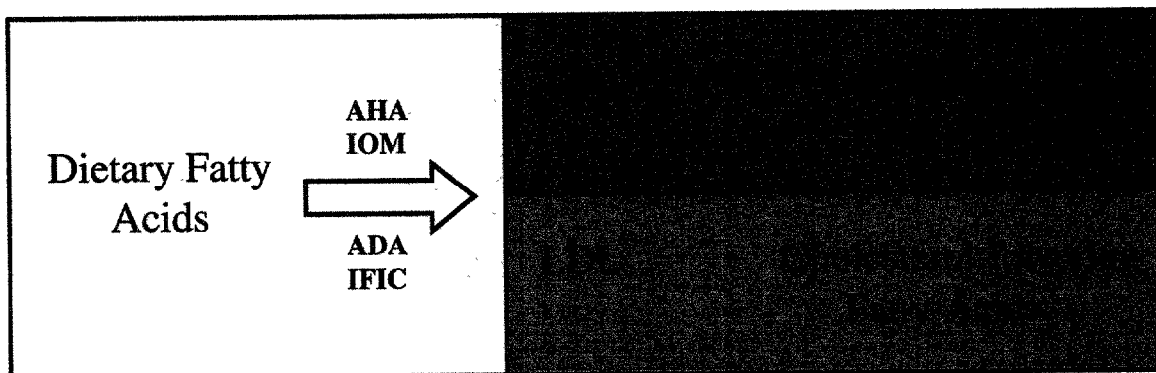
Consumer Messages about Cholesterol



Over time and with the support of major scientific organizations such as the American Heart Association (AHA) and medical organizations such as the National Cholesterol Education Program/Adult Treatment Panel III (NCEP), a new and more informative message about cholesterol was successfully introduced.

Attachment C

Consumer Messages about Fatty Acids



Various scientific organizations, e.g., the AHA, the Institute of Medicine (IOM) Dietary Guidelines Committee, and the American Dietetic Association, plus consumer information organizations like the International Food Information Council (IFIC) are in positions to help communicate key messages about the dietary effects of fatty acids.

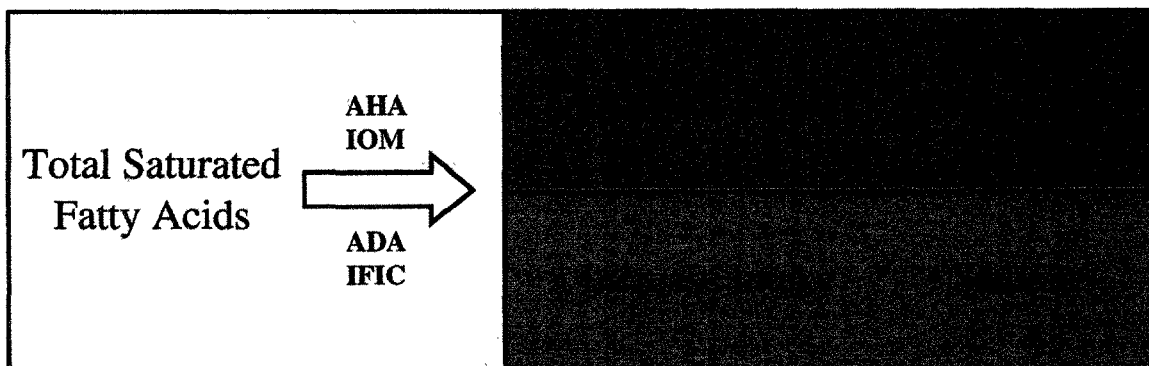
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Attachment D

New Consumer Messages about Saturated Fatty Acids



Organizations like IFIC have considerable experience in communicating science to consumers, for example see Borra et al (2001) Developing actionable dietary guidelines messages: dietary fat as a case study. *J. Am. Diet. Assoc.* 101: 678-684